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**CHILD AND ADOLESCENT PSYCHIATRY: PAST SCIENTIFIC
ACHIEVEMENTS AND CHALLENGES FOR THE FUTURE***

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Short Title: Child and Adolescent Psychiatry

* This article is based on an invited keynote lecture at an ESCAP-sponsored conference in 2009. The author was asked to provide a world-wide scientific history of research relevant for an understanding of psychopathology in childhood and adolescence and to conclude with suggestions for the future of the discipline in Europe. By design, the review excluded consideration of clinical services. The choice of scientific achievements to note was based on three criteria: 1) clear evidence of innovation; 2) widespread recognition of importance as judged by citations in leading reviews and textbooks; and 3) potential of relevance for clinical advances. Because the issues with respect to the future apply as much in other parts of the world as in Europe, the discussion of Europe-specific concerns in the keynote lecture has been omitted. During the preparation of the paper, three of the most important figures during the last half-century – Eisenberg, Garmazy and Robins died and this article is dedicated to them for the model of creative policy-relevant science and scientific integrity each of them provided.

ABSTRACT

The world-wide history of scientific achievements in child and adolescent psychopathology is reviewed from the mid 20th century onwards. Attention is drawn, for example, to diagnostic distinctions, measures of psychopathology, the several roles of epidemiological longitudinal studies, temperament and personality, developmental psychopathology, the use of ‘natural experiments’ to test causal inferences, environmental risks, the importance of gene-environment interplay, the relative coming together of initially diverse psychological therapies, the use of randomized controlled trials to assess treatment efficacy, and the value and limitations of pharmacotherapy. The article ends with a look ahead to the most important opportunities and challenges for child and adolescent psychiatry, plus the hazards that need to be avoided.

Although there were important roots in the 19th century and earlier, child and adolescent psychiatry only came of age as a recognized specialty in the 20th century [1]. It had its origins in the mental hygiene movement in the United States of America, a movement characterized by a multi-disciplinary emphasis, a child-welfare approach, and a focus on environmental causes. The term “child psychiatry” was probably first used at the Paris congress of 1934, but it had been preceded by the clinic in Heidelberg in 1926. Kanner’s text-book in 1935 provided the first English language systematic account of child psychiatry [2], although there had been several earlier German text-books which Kanner credited as having constituted an important influence [3]. There was the role of psychometrics as exemplified in the work of Binet [4] and there was the growth of psychoanalysis as an influence – accompanied

by vitriolic infighting between Melanie Klein and Anna Freud and their respective groups [5].

<H1> **MID TWENTIETH CENTURY LANDMARKS**

There were numerous important scientific contributions in the mid part of the 20th century. Their diversity may be illustrated by simply noting several examples. In many ways the most important of these was Bowlby's review [6] for the WHO on the effects of maternal deprivation. Whilst not all of his claims have stood the test of time, it was a revolutionary document that forever changed people's realization of the importance of children's experiences, and it led to radical changes in the patterns of care provided for children in hospital (including the introduction of the possibility of parents staying overnight, and the encouragement of frequent parental visits). This led on to Bowlby's trilogy on attachment [7, 8, 9] which was important in several different respects. To begin with, it was remarkable in its bringing together of quite diverse sources of evidence, both human and animal, and quite diverse theoretical perspectives. It alerted the world to the importance of the development of children's selective attachments in early life and the ways in which they provided the basis for later social relationships of all kinds. Also it led to key methodological advances by pioneers such as Ainsworth and Main [10].

Although Bowlby was the leading conceptualizer, the films made by James and Joyce Robertson [11] on children's behavior following admission to hospital made a huge impact and played a major role in altering hospital practices.

Levy's [12] study of maternal overprotection was outstanding in its analysis of what was involved in this form of parental behavior and particularly in his identification of the key features both in the child and in the parent that led to the development of overprotection and its psychological consequences for the child.

Many of the clinical studies undertaken at this time were of indifferent quality, but there were also some good examples of high quality research. For example, there was Hersov's [13] study of school refusal and Anthony's studies of encopresis [14] and of infantile psychoses [15]. Kanner's delineation of the syndrome of infantile autism in 1943 forever changed people's thinking, and it constitutes a splendid example of the insights provided by the very careful observations of an unusually astute clinician [16]. The follow-up studies taken up jointly by Eisenberg and Kanner [17] did much to increase understanding of the nature and qualities of this particular behavioral pattern.

The first randomized controlled trial was undertaken in the UK in 1948, investigating the use of streptomycin to treat Tuberculosis [18]. However, Eisenberg and Conners in the USA were pioneers in the 1960s in the use of randomized controlled trials to study the effects of treatments in the field of child and adolescent psychiatry [19].

In the first half of the 20th century, most clinicians and researchers paid little attention to the importance of diagnostic distinctions, but this was changed by Hewitt and Jenkins' [20] important factor analytic study of patterns of emotional and behavioral disturbance (which they termed "maladjustment"). This led to an acceptance of the need to differentiate between emotional disturbances on the one hand and disorders of disruptive behavior on the other hand.

<H1> VALUE OF LONGITUDINAL STUDIES

The first of the several UK-birth cohort studies was established in 1946 by Douglas [21], later led by Wadsworth. Amongst other things, it charted the continuities and discontinuities over time in patterns of psychopathology. Taken in conjunction with the later birth-cohorts established in 1958 and 1970, it also

established the possibility of examining changes over time in patterns of development and in the operation of risk factors.

The most important longitudinal study, however, was undoubtedly Lee Robins' [22], now classic, study of "Deviant children grown up". This showed important links between conduct problems in childhood and antisocial personality disorder in adult life; a demonstration of the links between psychopathology in childhood and exposure to adverse environments in adult life; and it established high quality concepts and measures that set the standard for all longitudinal studies that followed over the next half century. It was not the first long-term longitudinal study because there had been several predecessors – most notably the several Californian studies. Each of these made important contributions, but the Robins' study revived an interest in the use of longitudinal studies because it demonstrated so powerfully the ways in which such studies could be used to tackle really important questions about both nosology and operation of risk and protective factors. This led to the establishment of the international Life History Research Society in the 1950s which brought together some of the key researchers using longitudinal strategies who sought to learn from one another about matters of both methodology and substance [23].

In the years that followed, many more longitudinal studies were established around the world. The two studies in New Zealand – namely the Dunedin [24] and Christchurch [25] studies – are probably the best in the world because of the way in which they have been truly innovative in using longitudinal data to tackle crucially important questions of quite diverse kinds. However, equal credit must go to the quite different follow-up study by Sampson and Laub of Glueck and Glueck's [26] of a sample of seriously delinquent boys. The study is unique in the duration of follow-up to age 70 years [27], and is notable for its highly skilled combination of quantitative

and qualitative research methodologies, its methodological innovations, and the light that it has shed on both causes of psychopathology and protective factors operating in adult life through “turning point” effects.

A third set of longitudinal research strategies is provided by the various Scandinavian register-based follow-ups [28, 29]. They have capitalized on the existence of systematic national registers, and by the ability to link various register-based sources. Again, their use has been informative about risk and protective causal mechanisms.

Along with the development of crucial design features in longitudinal studies, there has been the development of a range of most important associated statistical devices. There are many, but particular mention must be made of the development of multivariate regression techniques, especially multi-level modeling [30, 31]. These have been important in dealing with the various issues that are implicit in nested studies (meaning that individual differences are embedded in family factors, community factors, and so forth). The other technique to mention is the development of growth-curve statistical models [32]. These have been important in enabling comparison of different growth-curve patterns and using these differences as a way of drawing conclusions about how risk and protective factors operate. Finally, of course, special mention must be made to the establishment of randomized-controlled trials. These have now become the ‘gold standard’ way of assessing the efficacy of interventions of all kinds. They were not primarily developed for use in psychiatry, but they have been hugely important within this field. Whilst they are not free of limitations (their strength lies in internal validity, and their limitations, particularly, lie in uncertainties about external validity [33] they have made a major impact on the assessment of evidence about which treatments work and for which conditions.

<H1> **KEY DEVELOPMENTS IN THE LAST 50 YEARS**

<H2> *Diagnostic distinctions*

Up until the 1960s, most psychiatrists paid very little attention to diagnostic distinctions. This was completely changed under the impetus of the Washington University group led by Eli Robins [34]. They changed the field because they showed how phenomenology could be used to make diagnostic distinctions, they set forth standards for establishing the validity of diagnostic distinctions, and they showed that diagnosis mattered. This approach led to what came to be described as the “Feighner” criteria, and the American Psychiatric Association’s (APA) DSM-III classification in 1980 used them as a basis [35]. During the 1960s and early 70s, the World Health Organization (WHO) held a series of international, interdisciplinary seminars to develop ICD-9. These did much to delineate areas of agreement and the areas where disagreements continued. Most important of all, they went on to show that most of the disagreements did not derive from differences in the way that clinicians perceived the clinical features but rather in the ways in which they used these features to fit in with theoretical preconceptions. In the child psychiatry field, this led to the development of a multi-axial classification of child psychiatric disorders that separated the clinical features from the associated risk and protective factors [36]. Its importance lay particularly in this approach having much in common with the way that most clinicians liked to operate.

This recognition of the importance of diagnosis was followed by the identification of some half a dozen new syndromes. For example, the fetal alcohol syndrome was identified first in 1973 [37], bulimia nervosa some ten years later [38], and attachment disorders were first introduced into DSM-III in 1980. Rett syndrome was first described in 1966 [39], but it did not make much impact at that time. Some

years later it was put on the map by Hagberg and colleagues [40], and is now recognized to be a quite distinctive condition caused by a single mutant gene and associated with a distinctive, unfortunately negative, course. Post-traumatic stress disorders (PTSD) had been recognized since the early years of the 20th century, but they were first clearly conceptualized in Vietnam veterans and were then first applied to children in DSM-III-R in 1987 [41]. Quasi-autism as a syndrome associated with profound institutional deprivation was described first in 1999 [42]. It is most noteworthy that all of these new syndromes derived from clinical observations and not from the application of basic laboratory research findings. Currently, there is a great deal of interest in trying to translate basic science into clinical practice. However, one must not lose sight of the fact that there is a two way interplay between clinical observations and basic science, and not just a one way traffic [43].

<H2> *Epidemiology to plan services and study risk factors*

The Isle of Wight epidemiological studies led by Tizard, Whitmore and Rutter in the late 1960s and early 1970s were associated with a number of crucially important innovations [44, 45,46]. To begin with, the studies were planned with the twin objectives of planning services and studying causal risk factors. The studies established the value of systematic interviewing of children, which had been rejected prior to this point as a waste of time. They established the frequency of co-occurring patterns – so called, comorbidity. They established the causal role of organic brain dysfunction of mental disorders in childhood, they demonstrated marked school variations in rates of disorder, they showed the important psychopathological risks associated with family dysfunction, they showed marked area differences in rates of disorder, and they indicated the problems in the widespread concept of so called

‘adolescent turmoil’. More generally, they showed the importance of systematic, standardized methods and measurement.

The Isle of Wight studies were followed by the Waltham Forest study [47] which was instrumental in showing that preschool psychopathology was often a precursor of later disorders. This was important because, hitherto, preschool problems had been rather dismissed as being of little long-term significance. The Isle of Wight findings on school variations and rates of disorders led on to the systematic studies undertaken by Rutter, Maughan, Mortimore and Ouston in inner London of school effectiveness (these used epidemiological/longitudinal research strategies and were innovative in showing the importance of studying variations in patterns of intake to schools) in order to identify the influence of schools on pupil outcomes [48].

<H2> *Measures of Psychopathology*

Although not constituting a scientific advance in their own right, the development of structured interviews – both respondent-based [49] and investigator-based [50, 51] have been crucial in providing the instruments for scientific advances. There has also been the development of screening questionnaires, of which the Child Behavior Check List (CBCL) is the best developed [see 52, 53]. These have been used in many epidemiological studies but are not suitable for individual diagnosis.

<H2> *Establishment of the value of developmental psychopathology*

It might be thought that developmental perspectives had always been a prominent part of conceptual thinking in relation to child and adolescent psychopathology, but, in reality, this was far from the case before the 1970s. The value of considering psychopathology from a developmental perspective was argued persuasively in key papers by Garnezy, Sroufe and Cicchetti as well as by Rutter [see 54]. Each of these approached the issues in a somewhat different way, but they came

together in an agreement that it was necessary to consider both continuities and discontinuities over behavioral variation (i.e., recognizing that there was much to be gained from considering similarities and differences between normal development and mental disorder), and continuities and discontinuities over developmental course (recognizing that it could not be assumed that either continuity or discontinuity was normative).

Several rather distinct bodies of research played key roles in conceptualization of developmental psychopathology. Thus, longitudinal studies had shown the neurodevelopmental origins of both autism [55] and schizophrenia [56]. Adult psychiatrists had originally conceptualized schizophrenia as an adult psychosis for which development in childhood was utterly irrelevant. It is now very clear that this is very far from the case. Individuals who later develop schizophrenia have been found to show impairments in the early development of both language and motor functions. Similarly, autism was found to be followed in about 20% of cases by the development of epileptic seizures, usually in adolescence or early adult life. In addition, basic cognitive deficits were found to be part of the core problem. Rapoport and colleagues [57, 58] showed age differences in young people's response to drugs, both prescribed medications and illicit recreational use. Surprisingly, this observation has been little investigated and that remains a key priority for the future. Age differences in children's responses to lateralized brain injury affecting parts of the brain concerned with language alerted people to the importance of plasticity in development [59]. At one time, it was thought that the effects of brain injury in early life were less damaging than those in later life, but that proved to be a mistaken notion. It is not that the effects of brain damage vary in severity by age, but rather that their patterning is different. Moreover, the main difference is between the early

years of childhood and adolescence and later, rather than with childhood as a whole. At about the same time period, basic research by Hubel and Wiesel was showing the importance of sensory input to the development of the visual cortex [see 60 for their collected papers].

The work of Brown and Harris [61] was important in identifying the impact of early life vulnerability factors in influencing children's response to later acute life stressors. Clinical studies had long identified the possible role of early life experiences in relation to the risk for later mental disorders, but a major step forward was taken by the use of "natural experiments" to test in rigorous fashion the causal inference [62]. The work of Kendler and Prescott stands out in this connection in relation to investigating the long-term sequelae of sexual abuse [63]. The Dunedin longitudinal study, as used by Kim-Cohen and her colleagues, was influential in showing that a majority of mental disorders of sufficient importance to lead to treatment in early adult life had actually already been manifest in childhood [64]. Barbara Maughan [65] used a follow-up of the Isle of Wight sample to show that reading problems in childhood were followed by a markedly increased rate of spelling difficulties.

<H2> *Temperament, personality and personality disorder*

The history of an interest in individual differences in temperamental features extends back to the 19th Century – especially in the German-speaking literature [66]. The contributions of Kretschmer and Stern were particularly important in the first half of the 20th Century. The application to child psychiatry, however, was pioneered by Thomas, Chess, Birch and their colleagues [67]. The study of biology of temperament was particularly taken forward by Kagan [68, 69] and Rothbart [70] but numerous other investigators made important contributions [71]. Both developed an

important 4 dimensional questionnaire measure of temperament and conceptualized temperament as inherited traits that appeared early in the first year and remained stable over time. Neither of these concepts has proved fully correct but they served to put temperament on the map. Research during the last few decades has focused on four key issues. First, there is the evidence on the longitudinal course of temperament – showing very low predictive power from the infancy period, substantial stability from age 3 years, but continuing changes even in adult life [72]. Second, prompted by Bell's [73] challenge on the role of child effects in socialization studies, there has been investigation of the effects of children's behavior on eliciting responses from other people [74]. Third, there was a recognition of the need to consider the connections between personality and personality disorders [75] with an appreciation that some personality disorders, such as schizotypy, are best conceptualized as a variant of a psychiatric condition (in this case schizophrenia) rather than a variant of temperament or personality [76]. Finally, there has been the research showing that psychopathic features are identifiable in childhood [77] and that they are highly heritable [78].

<H2> Development of focused psychological therapies using problem solving strategies

The first important study was that undertaken by Reid and Shyne [79] in which they examined the relative value of time-limited focused approaches, and more open-ended long-term methods. The findings were striking in showing the advantages of a focused approach. Similar findings came a few years later from the research undertaken by Kolvin and his colleagues [80] in the U.K. Brief psychotherapy, as used with adults, was pioneered by Malan [81], and problem

solving methods as used with children by Shure and Spivack [82]. Beck [83] was the key pioneer in the development of cognitive-behavior therapies (CBT) in adults, and Meichenbaum and Goodman [84] were the pioneers in developing CBT with children. Focused parenting programs were developed by both Webster-Stratton [85] and Patterson [86], with a range of innovations in techniques, accompanied by systematic evaluations of efficacy.

Historically, psychodynamic, psychoanalytically influenced, long-term interventions were sharply discrepant from the highly focused behavioral interventions developed by psychologists. Although important differences in psychological therapies remain, there has been a very considerable coming together. Psychodynamic psychotherapies have recognized the importance of real life experiences, and behavior therapists have recognized the importance of thought processes. In both cases, there has been an appreciation that there has been much to be gained by short-term focused approaches with definite objectives in mind.

Over the same period of time, multiple family therapies were developed [87]. These suffered substantially from ideological commitments and disagreements among the various schools of family therapy. Nevertheless, the development of family methods was important in an explicit focus on real life family interactions and the expectation that families would undertake problem-solving tasks during the intervals between therapeutic sessions. In recent years, too, there has been the development of various attachment therapies that share some of the qualities outlined above [88]. For example, they focus on real life interactions and there is a focused approach in time-limited interventions.

<H2> *Use of pharmacological treatments and randomized controlled trials*

There are several rather different aspects of the advances that have taken place in the evaluation of pharmacological treatments. The recognition of the importance of using randomized controlled trials has already been mentioned, but there are several other important advances that made a difference in conceptualization. Thus, at one time, the therapeutic benefit brought about by the use of stimulant medication in the treatment of ADHD in children was assumed to represent a paradoxical response. That is to say, it was assumed that the response was qualitatively different from that found in normal individuals. The research undertaken by Rapoport and her colleagues [57, 58] was crucial in indicating that this was not so. Stimulants did indeed have an effect in improving attention in children with ADHD, but similar effects were also found in normal children. This did not mean, of course, that stimulants should be used in normal children (because they did not have the problems of inattention that warranted pharmacological intervention), but the findings did force people to consider the mediating mechanisms. Longitudinal studies showed the strong continuities between depression in children in adolescence and major depressive disorders in adult life [89], and it was therefore surprising that it was found that depression in childhood was not responsive to the tricyclic antidepressants that brought substantial benefits to adults [90]. On the other hand, the SSRIs did seem to be effective in the treatment of depression in young people [91] (although, more recently, concerns have been raised about possible side-effects in terms of an increase in suicidal tendencies).

There are three issues that have begun to receive increasing scientific attention in the field of neuropharmacology. First, there is the question of why people differ so markedly in their response to the same medication –both in terms of drug efficacy and side-effects. One possible answer may lie in the realm of molecular

pharmacogenomics [92]. So far, the replicated findings mainly concern individual differences in drug metabolism, but genetic differences in response to different drugs could prove even more clinically useful. The problems involved in making ‘individualized medicine’ a practicality in the case of multifactorial disorders, however, are numerous and may not be achievable [93]. Second, there is the question of which drug action provides the drug efficacy. The topic is very important because nearly all drugs tend to have actions on multiple neurotransmitters. The third, related, query is why there are such minor differences in the clinical efficacy of different psychotropic drugs. The break-through has come through the use of positron emission tomography (PET scans), using radio-labeled ligands to examine the degree of neurotransmitter receptor occupancy. The work of both Kapur et al. [94, 95] and Volkow et al. [96,97] well illustrate the strategy as a means of providing a better understanding of drug efficacy.

At a more general level, there was the development of a widespread recognition that small-scale individual therapeutic studies were not going to provide adequate answers. Multi-site collaborative studies were essential, and have been undertaken with respect to the treatment of both depression [98] and ADHD [99]. Such studies, of course, require not only cooperation between different centers, but also very careful planning and monitoring to ensure that the same methods of measurement are used in the same way in each centre.

<H2> *Recognizing the importance of genetic influences and of G-E interdependence*

This has been one of the major growth areas in research over the last few decades, and it is possible only to pick out selectively a few key highlights. The first systematic twin study of autism by Folstein and Rutter [100,101] warrants mention, not just because it indicated for the first time that genetic influences were very

important in the liability to autism (which many previously considered a psychogenic disorder), but more particularly because the findings showed that the genetic influences applied to a broader phenotype than that presented by the traditional severe, handicapping disorder of autism, and that the genetic influences operated in a multifactorial, probabilistic fashion rather than the determinative way in which single gene Mendelian influences operate. At the time, there was some resistance among geneticists to the departure from Mendelian assumptions, and the focus on a broader phenotype, but both are now accepted, not only in relation to autism, but much more broadly in the field of psychopathology.

During the latter part of the 20th century, a huge number of twin and adoptee (as well as family) studies showed that genetic influences operated on virtually all forms of mental disorder, albeit to differing degrees [102]. In addition, attention moved away from the assumption of determinative direct effects on mental disorder to the recognition of the importance of indirect genetic influences. Thus, Plomin and Bergeman [103] used quantitative findings on gene-environment correlations to argue that some of the risk effects of environmental features were actually genetically, rather than environmentally, mediated. It took a little while for psychosocial researchers to accept the reality of this issue, but it now has become generally accepted. Quantitative genetics had also pointed to the likely operation of gene-environment interactions [104]. Researchers and clinicians became aware that genetic influences often operated through genetic effects on environmental risk exposure (through gene-environment correlations) and differences in environmental susceptibility (operating through gene-environment interactions).

The study of GxE was revolutionized, however, when molecular genetic methods were used to identify individual susceptibility genes and when there was

good measure of environmental features. A series of seminal papers based on the Dunedin study published by Caspi, Moffitt and their colleagues [105,106] showed the importance of such effects and also outlined the strategic approach needed to investigate GxE. There are three other advances that were crucial in providing some better understanding of gene-environment interdependence. First, there was the use of animal models which were useful in demonstrating in primates that similar GxE effects were operative [107, 108]. Second, there was the experimental study of the neural effects of GxE in humans led by Weinberg, Meyer-Lindenberg and Hariri [109]. Structural and functional brain imaging techniques were used in conjunction with molecular genetics for this purpose. Interestingly, and importantly, these studies focused on effects in individuals without evidence of psychopathology. The fact that the neural effects were found in these participants was crucial in showing that the biological pathways had to be ones that operated more generally than just in individuals with significant disorders. The third advance was provided by the research of Meaney and his colleagues [110] in demonstrating the epigenetic mediation of environmental effects. Although environments cannot influence gene sequences, they can and do influence gene expression, and this realization opened the way to a study of environmental moderation of genetic effects – thereby highlighting a rather different form of gene-environment interdependence.

<H2> Role of cognitive processes in social functioning

The pioneers in the sphere of cognitive processes and social functioning were undoubtedly Hermelin and O'Connor [111] through their program of research examining autistic children's use of meaning in memory. They were the first to clearly identify mentalizing problems, but research was limited by the difficulty at that time in indicating how this might operate in the liability to autism. The next step

forward was provided by the demonstration of so called 'Theory of Mind' deficits in autism by Frith, Baron-Cohen and their colleagues [112]. This research was based on studies of the role of 'Theory of Mind' in normal children and, like the earlier research of Hermelin and O'Connor, the findings pointed to important parallels between normal and abnormal development [113]. The benefits of using the study of normal development to cast light on processes in mental disorders and the converse of using studies of individuals with psychopathology to understand normal development became firmly established. One limitation of the 'Theory of Mind' work was that, at least as measured at that time, the emergence of 'Theory of Mind' emerged too late to explain the social abnormalities in autism that were evident before the age of two. Research turned to the role of eye gaze and of joint attention as features that might be important, and indeed proved to be so [114]. Whether or not these are precursors of 'Theory of Mind' or whether they represent a rather different cognitive pathway is not yet entirely clear.

Another rather different research strategy focused on similar issues was provided by the use of sibling studies to investigate the early manifestations of autism [115]. The rationale here was that the siblings of individuals with autism were likely to develop an autism-spectrum disorder themselves in some 5-10% of cases.

The development of functional brain imaging techniques proved crucial in opening up the opportunity to study brain-mind interconnections. In the field of autism, these were instrumental in showing that the disorder did not lie in a localized abnormality in one part of the brain but, rather, a lack of normal connectivity across brain systems [116]. However, in addition, such methods have shown a whole range of different ways in which brain-mind relationships can be studied.

Finally, mention must be made of Rizzolatti's discovery of mirror neurons [117]. These are neurons that respond to individual's perceptions of what another person is doing or might be doing. Their importance lies in the possibility that impaired function of these mirror neurons might constitute the neural basis of autism. One difficulty in testing this notion is that the mirror neurons are rather widely distributed in the brain. However, useful steps have been taken in trying to link mirror neuron activity with social functioning.

<H2> *Recognition of role of social context*

At one time, most discussion of the role of lack of social influences on the liability to psychopathology concentrated on family interaction with the implicit assumption that these family effects operated independently of the broader social environment. Bronfenbrenner [118] was the pioneer who changed all of that in his discussion of ecological concepts of the ways in which environments were nested within broader arenas. Thus, there was the role of the individual, which was nested within the family, which in turn was nested within the community, and so forth. This appreciation had an influence on the concepts of how psychosocial influences operated, but also had crucial implications on the use of multi-level modeling to investigate such influences.

The demonstration of area variations in rates of crime and in rates of psychopathology goes back to the middle of the last century [119]. Conceptualization of how these variations worked did not move forward very much until the important study by Sampson and his colleagues in Chicago [120]. The findings suggested that the area effects derived less from qualities that pushed people towards crime than influences, associated with social disorganization, that failed to inhibit antisocial behavior. The Moynihan report [121] highlighted both the existence of ghettos and

their role in predisposing individuals to criminal behavior. At the time the report was published, it got a very negative reception from many commentators who read into the report all sorts of values that actually were not there. A recent re-evaluation of the report [122] has served to confirm the validity of many of the arguments put forward by Moynihan.

Research into the effects on children of differences among schools in their effectiveness was put on the map by Rutter and his colleagues [48, 123]. Two key features were especially important. First, the use of longitudinal data made it possible to determine whether the variations among schools in pupil outcomes was simply an artifact of differences in pupil intake; it was found that it was not. Second, systematic measures of how the school functioned made it possible to identify the distinctive school features associated with greater effectiveness. Somewhat similar methodological issues applied to the possible role of antisocial gang membership in fostering increases in criminal behavior. The work of Thornberry and colleagues [124, 125] stands out with respect to the use of longitudinal data to sort out selection effects and social influence effects. Both were found to be operative but it is the demonstration of within-individual changes over time that provided the first convincing evidence of a causal effect.

Clinicians and researchers have been aware for a long time that there are quite strong ethnic variations in rates of psychopathology and psychological functioning more generally. Unfortunately, most of the earlier research was based on the misguided assumption that comparisons had to be made with a normative, Caucasian situation. It is now appreciated that this is a prejudicial approach and also that it gets in the way of understanding the mediating mechanisms. Rutter and Tienda [126] brought together a set of interdisciplinary, international essays, all of which served to

show that the study of ethnic variations need not be prejudicial; indeed to the contrary they could be very informative in leading to the identification of the influences that mediated variations and, moreover, that findings could well be informative with respect to the broader population and not just to the particular ethnic minority group being studied.

<H2> *Use of “natural experiments” to test hypotheses on environmental mediation*

Campbell was the pioneer in outlining the range of different forms of “quasi experiment” that could be used to test hypotheses on environmental mediation of causal influences [127]. The need for such approaches derives from the fact that there are several key threats to the causal inference, such as those deriving from genetic mediation, from social selection, from reverse causation, and from unmeasured confounding variables [see 62, 128]. A range of twin, adoptee and migration strategies have been used to exclude genetic mediation, with Kendler [63], Caspi [129] and Plomin [102] being among the pioneers here. There are then a variety of designs that may be used to contrast different types of environmental mediation, so enabling avoidance of the misidentification of causal effects [63]. Designs using universal exposure are valuable in controlling for social selection [130] as are regression-discontinuity designs [131]. The use of these “natural experiments” served to pull apart variables that ordinarily go together, and they have been effective in confirming some postulated causal effects and excluding other causal claims.

For example, the study of discordant twin pairs showed that the twin exposed to sexual abuse had a greatly increased risk of later mental disorder – thus showing the environmentally mediated causal effect stemming from sexual abuse [63]. Multivariate twin analyses showed that physical abuse had an environmentally mediated causal effect on mental disorder, whereas corporal punishment did not

[132]. A range of natural experiment designs have confirmed the prenatal effect of maternal smoking on birth weight but cast doubt on the claimed prenatal effect in causing either antisocial behavior or attention deficit disorder with hyperactivity (ADHD) [133]. The study of institution-reared children from Romania adopted into UK families showed that the initial developmental deficits were indeed due to the deprivation (because they remitted after removal from the institution) and that deprivation led to persisting disorders of an unusual kind (such as quasi-autistic patterns or disinhibited attachment [134, 135].

<H2> The rise of anti-science ideologies, and the misleading claims of biological determinism

For quite some time, psychoanalysis acted like a religion with claims assessed in terms of ideological tenets, rather than either logic or empirical evidence [5]. Because of this, psychoanalysis was to psychiatry what creationism is to biology. The issue is not whether their particular claims were or were not correct, but rather that the ideological approach took psychoanalysis outside the boundaries of science. This was accompanied by Winnicott's claim [136] that clinical training was irrelevant and that research was damaging. At about the same time, Bettelheim's [137] 'blame the parent' agenda meant that many parents were wrongly charged with being responsible for their child's autistic problems [138]. Somewhat similar ideological features were somewhat evident in the early days of family therapy, and in some of the current claims on attachment. All of this was followed by the equally misleading claims of biological, or genetic, determinism.

It is necessary, in order to avoid misunderstandings, to make explicit that individual psychoanalysts made important contributions to the development of psychological therapies and, also, that some of the claims of psychoanalysis (such as

the existence of mental mechanisms) have proved valid. The damage came from treating a theory as a religion in which there was rejection of any use of non-psychoanalytic methods to test psychoanalytic claims, an insistence that practitioners had to undergo a personal analysis in order to be accepted, and that disputes regarding psychoanalytic theory had to be resolved by reference to the ‘high priests’ of the psychoanalytic world rather than by any form of dispassionate assessment.

<H2> *Moving on in concepts and therapeutic approaches*

We need to pay attention to Eisenberg’s [139] warning that we should not replace a “brainless” psychiatry with a “mindless” psychiatry. The point he was making was that in the era when psychoanalysis dominated, everything was assumed to operate in terms of mental operations that had got nothing to do with the biology of brain functioning. Quite rightly, that narrow minded approach has been rejected, but he was warning that there is now a parallel danger that we are running the risk of focusing exclusively on neural functioning without appreciating that we have evolved to have a mind that allows us to look back, to plan, and to look ahead. For all its faults, psychodynamic therapies led therapists to listen to patients and to appreciate that role of mental mechanisms. Initially, the emphasis was entirely in terms of patient’s thinking and not in terms of their real life experiences; however, as I have tried to indicate, the advances in psychological therapies have incorporated much more in the way of paying attention to actual experiences (both in the past and in the present) and to take problem-solving approaches of a systematic kind. There has been a relative coming together of different types of psychotherapy, together with a greater attention to evidence and the need to evaluate the efficacy of preventive and therapeutic interventions [140].

Whilst there is every reason to suppose that a developmental perspective is important (as indicated by the evidence from developmental psychopathology), we also have to agree with Bowlby's [141] assessment that psychoanalysis was never more wrong than in its theory of child development. That is not its important contribution, and it is time to put aside those aspects of psychoanalysis.

Following on from the recognition in the 1970s of the importance of diagnostic distinctions, there came the development of many forms of standardized interviews relying on different forms of structure. There can be no doubt about the value of these systematic interviewing methods in both research and in clinical work (see above). On the other hand, there is a very real danger that a blinkered adoption of structured diagnostic interviews will interfere with attention to patient's concerns and needs, to assessing strengths and weaknesses in the family and broader social situation, and in planning approaches to treatment. Diagnostic assessment should not be confined to just coming up with the "correct" diagnostic label. This is not just a private value judgment because systematic studies of different approaches to interviewing have shown the frequency with which there are clinically important pieces of unexpected information that fall outside the scope of the structured interview [142].

<H1> **KEY OPPORTUNITIES IN CHILD/ADOLESCENT PSYCHIATRY**

In this historical overview of the worldwide scientific achievements of the last 50 years relevant to an understanding of the causes, course or treatment of mental disorders, it is evident that an enormous amount has been achieved. It is also clear that many of the major steps forward came from psychologists, sociologists, geneticists and others from non-psychiatric disciplines. Moreover, even when focusing on child psychopathology the contributions of adult psychiatrists are at least

as great as those of child and adolescent psychiatrists. Finally, the major advances have come from many different countries. We need to ask ourselves whether, given that the best modern clinical and basic sciences are both international and interdisciplinary, it is still appropriate to have single discipline, regional organizations. There may be value if these are predominantly aimed towards self-help, but we need to look outwards and not inwards.

With respect to training in child and adolescent psychiatry, it is good that this has become both more systematic and evidence-based [see 143] for a review of the state of play in Europe a decade ago). Nevertheless, where there are exams in psychiatry to be passed, we need to query the increasingly exclusive focus on ‘facts’, with little or no attention to concepts and ideas. This has come about because of the greater ease of marking reliably tick-box correct or wrong answers. Of course, there are crucial facts that must be mastered but we need to remind ourselves that history teaches us that of the ‘facts’ learned, by the completion of training, about a third will later prove to be correct, but another third will have been found to be wrong, and a further third correct but not very relevant. The dilemma is that, at any one point in time, we do not know which facts fall in each third. A change of approach is needed if we are to foster continuing learning over the course of a person’s professional career. With these features in mind, we need to consider the challenges still before us.

Genetic evidence is consistent in showing that there are major environmental effects on the liability to mental disorders, as in adult life. The excitement of the important technologies that are now available to use in research must not blind us to the appreciation that the environment has very important effects. On the other hand, there is the need to take seriously the testing for environmental mediation. This will

continue to involve “natural experiments” as well as employing laboratory manipulations [62].

In particular, there is a need to determine the biological basis of environmental effects that persist beyond the period of exposure to stress/adversity [133]. That is, we have to undertake the appropriate research to determine how environments “get under the skin”. In seeking to understand this biological basis, we will need to contrast epigenetic, neuroendocrine, and mental model mechanisms to mention just three out of a broader range of alternatives. It is much too early to take decisions that any one of these is going to prove to be the predominant mediating mechanism.

Equally, there is a need to delineate the biological mediating mechanisms involved in gene-environment correlations and interactions [144]. In other words, we need to study the indirect effects of genes, a process that is sometimes expressed in terms of how genes get “outside the skin”. This will involve understanding how the behavior of individuals acts to select and shape environments. Such research needs to have a focus on the role of these individual behaviors, with the determination of the extent of genetic influences as a secondary, rather than a primary, consideration. By contrast, the study of genetic effects on susceptibility to environmental causes requires genetic research strategies. As discussed, these need to use molecular genetic strategies to identify individual genes and to have good quality measures of relevant environments. If we are to understand the neural basis of GxE, it will be necessary to undertake experimental brain imaging studies using specific genes and intermediate phenotypes. The latter are important in order to study the immediate effects of GxE without waiting decades for psychopathology to develop. The way ahead in this connection has already been demonstrated [109], but more research of this kind is needed.

There is also a need for the development and use of animal models. Up until now, these have played rather a small role in child and adolescent psychiatric research, but they have an important place. Of course, there are many difficulties in devising appropriate animal models, but they provide a crucially important way of testing apart aspects of causal mechanisms [145, 146].

Longitudinal studies of high risk groups are required in order to identify the mechanisms involved in transitions across developmental changes in psychopathology [64]. Thus, this is needed when studying how the prodromata of schizophrenia lead on to schizophrenic psychoses in some individuals but not in others. Similar needs apply to the transitions from the broader phenotype of autism to a seriously handicapping disorder.

There is certainly a need for more, and better, studies of treatments (both psychological [140] and pharmacological [98,99]); these need to be accompanied by designs that can test the mediators of therapeutic effectiveness and the causes of individual differences in response. Pharmacogenetics provides one important focus with respect to individual differences, but a broader range of strategies need to be employed. There is an especial need to identify the mechanisms involved in age differences in response to drugs and to major hazards. It is decidedly curious that these issues have received so little systematic research attention up until now.

Past research has provided many pointers on possible modes of prevention of child and adolescent psychopathology, and there is a certain amount of evidence that well planned preventive measures can be effective [147, 148]. Developing further preventive strategies, it will be important to take on board the fact that most forms of mental disorders in young people (as in adults) are recurrent or chronic, as well as recognizing the need to consider the biology [149]. Accordingly, evaluations must be

concerned with long-term effects (both beneficial and damaging); planning also needs to be sensitive to the times when preventive interventions may be effective and when they will be received positively by those to whom they are offered.

With respect to both preventive and therapeutic interventions, we need to appreciate that causation often, and probably usually, involves multiple pathways. This is nothing special to psychopathology but is something that applies across the whole of biomedicine. It has come to be accepted, too, that most genes have pleiotropic effects and that most environmental influences also affect a range of different outcomes [146]. Currently, there is much attention to the issue of supposed comorbidity, but it needs to be appreciated that much of this co-occurrence is likely to be artifactual, and that the identification of co-occurrence is a starting point for research and not an end point. Insofar as the effects are real, we need to determine the mechanisms involved. There is not a single research strategy that is appropriate for this task, but what is clear is that research designed to pit alternatives one against another is likely to be the most informative.

In that connection, it is also obvious that the official classification systems contain far too many individual diagnoses. There are many of these diagnoses that are rarely, if ever, used, and it is quite impractical to suppose that even the most skilled and experienced clinicians can carry in their head the rules required to make some 400 or more diagnoses. It is very much to be hoped that the currently ongoing revisions of the ICD and DSM classifications will simplify systems as well as making them more scientifically validated and more clinically useful. This will need to include attention to the coverage of preschool disorders, and especially the development of diagnostic systems that are usable in primary care (both medical and non-medical) where time and resource requirements mean that simplified procedures

are essential. One specific issue that will require attention is the use of dimensions. On the one hand, there is much evidence across the whole of biomedicine that there are dimensional features to most disorders, and that most risk factors operate dimensionally, rather than categorically. On the other hand, clinical decision making has to involve categorical decisions. It makes no sense to think that you can have a little bit of medication or a little bit of hospital admission. Accordingly, it is to be hoped that dimensions will form a part of diagnostic approaches, but that careful attention will be paid to finding workable ways of coming to categorical decisions.

Post mortem studies have proved of value in the study of disorders in adult life and, potentially, they should be informative with respect to mental disorders in childhood [110, 150]. Practical problems stem from the fact that most young people with mental disorders do not die young and when they do die young they are often atypical in many crucial respects. There are also the practical problems associated with the fact that most deaths in early life are unexpected and have to be subject to scrutiny by Coroners. Nevertheless, it is important that brain-banks be established and used in a collaborative manner.

There are several issues that are new and of high importance in the field of genetics. For example, there is now good evidence that copy number variations (CNV; meaning submicroscopic deletions and substitutions within DNA sequences) play a causal role in relation to both autism and schizophrenia (and probably other conditions as well) [151]. Two major issues require attention. First, most CNVs are not familial and arise *de novo*. This means that although they can be demonstrated to play an etiological role, they do not account for familiarity. In addition, even when there is a familiarity, it is clear that the effects are probabilistic and not determinative because some family members with the CNV do not show the condition being

studied. The second issue is a different one and concerns why the rates of CNVs (and also chromosome anomalies and minor physical anomalies) are much more common in the individuals with autism or schizophrenia than they are in the general population. The likelihood is that they arise randomly through stochastic variation, but what are the non-genetic factors that make such variations more likely? One possibility being investigated is raised parental age [152], but there are other possibilities. Out of the same areas of research, there is discussion now of the relative importance of rare and common variants with respect to genetic influences. The related issue is that many of the rare variants are associated with somewhat atypical phenotypes with an uncertain relevance for the broader run of conditions. In addition, we need to ask why with conditions such as autism or schizophrenia, in which there is markedly reduced fecundity, do not become eliminated and extinct [153]. We do not have satisfying answers to that query at the moment, but we do need to appreciate that conditions associated with markedly reduced fecundity may involve somewhat different genetic mechanisms than in those where that is not the case. Expressed more generally, we need to move away from an exclusive focus on gene hunting to search for an understanding of the biological mechanisms that are implicated in genetic effects. That will certainly have to involve basic science strategies focused on determining on what genes ‘do’ in terms of effects on proteins and, even more crucially, how those protein effects lead on to the phenotype being considered.

<H1> **PROBLEMS AND CONCERNS REGARDING THE FUTURE**

As is implicit in all that has been said with respect to the past, it is essential, in the future, to avoid the ideologies that seek to escape the need for empirical evidence. That applies as much to pharmacological evangelism and biological determinism, as to psychoanalysis, family therapy and attachment theory [139]. Second, we need to

work with industry because their involvement is going to be essential in drug developments but, equally, it is crucial that we guard against the biases and control (as well as the personal greed) that may come in with the tide [154]. Third, we have to avoid reliance on single treatment methods. That applies even to methods, such as CBT, that have proven efficacies in certain circumstances. The point is that there is no treatment that provides the “silver bullet” and deals with all the problems and, moreover, developments in science may bring new circumstances for which the currently favored treatment is no longer the method of choice. Clinical training has to involve an appreciation of diverse treatment approaches and not just one.

Finally, we need to recognize that, in recent times, child and adolescent psychiatrists have played a rather limited role in the major areas of innovative research. I have indicated some important exceptions, and there are many more that I could have listed. Also, of course there are many more now doing very good research (albeit not innovative to the extent required for inclusion in this review), but there is a paucity of people doing top level international research likely to open up new avenues and challenge the ‘wisdom’ of the day. It is this sort of creative iconoclastic that I have focused on in my historical overview and it is those who are in short supply. Adult psychiatrists and psychologists have increasingly taken over leadership in many of the high-priority areas. Their involvement is positively to be welcomed and it would be quite wrong to seek to marginalize them. To the contrary, their leadership has been a major positive benefit for child and adolescent psychiatry. Even so, we have to act to ensure that future generations of child and adolescent psychiatrists include really able individuals who receive systematic research training, and who are capable of moving in a creative fashion to develop new concepts and new approaches.

I conclude that there is much that is good in both child and adolescent psychiatry research and clinical services, but there are important weaknesses that require remedial action. Steps are being taken to strengthen the discipline and all of us must play our part in doing all we can to further strengthen research and the clinical practice so that the younger generation is in a position to move strongly ahead in the future.

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